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Health and Environmental Effects Profile for Chrysene

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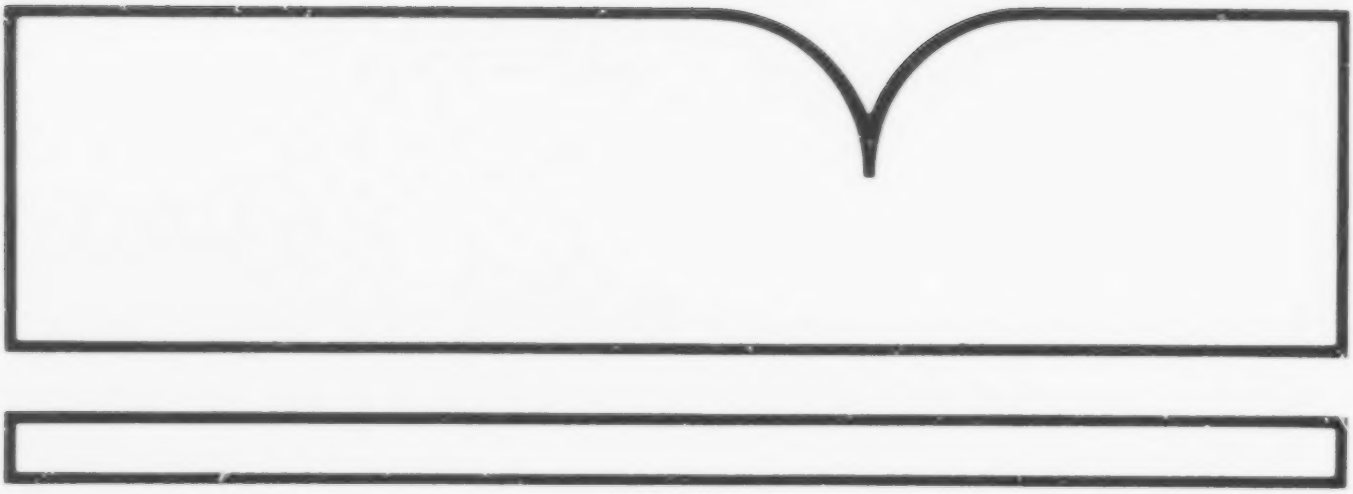

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HEALTH AND ENVIRONMENTAL EFFECTS PROFILE FOR CHRYSENE

ENVIRONMENTAL CRITERIA AND ASSESSMENT OFFICE
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16. ABSTRACT

The Health and Environmental Effects Profile for chrysene was prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA). Both published literature and information obtained from Agency program office files were evaluated as they pertained to potential human health, aquatic life and environmental effects of hazardous waste constituents.

Quantitative estimates have been presented provided sufficient data are available. Existing data are insufficient to determine an Acceptable Daily Intake (ADI) or a carcinogenic potency factor for chrysene.

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PREFACE

Health and Environmental Effects Profiles (HEEPs) are prepared for the Office of Solid Waste by the Office of Health and Environmental Assessment. The HEEPs are intended to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA). Both published literature and information obtained from Agency program office files are evaluated as they pertain to potential human health, aquatic life and environmental effects of hazardous waste constituents.

Quantitative estimates are presented provided sufficient data are available. For systemic toxicants, these include, Acceptable Daily Intakes (ADIs) for chronic exposures. An ADI is defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect. In the case of suspected carcinogens, ADIs are not estimated in this document series. Instead, a carcinogenic potency factor or q_1^* is provided. These potency estimates are derived for both oral and inhalation exposures where possible. In addition, unit risk estimates for air and drinking water are presented based on inhalation and oral data, respectively.

The first draft of this document was prepared by Syracuse Research Corporation under EPA Contract No. 68-03-3228. The document was subsequently revised after reviews by staff within the Office of Health and Environmental Assessment: Carcinogen Assessment Group, Reproductive Effects Assessment Group, Exposure Assessment Group, and the Environmental Criteria and Assessment Office in Cincinnati.

The HEEPs will become part of the EPA RCRA docket.

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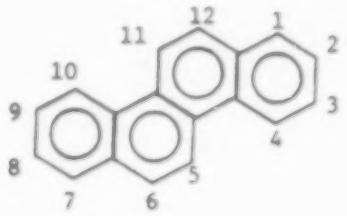
LIST OF ABBREVIATIONS

ADI	Acceptable daily intake
AUC	Area under the curve
BCF	Bioconcentration factor
DNA	Deoxyribonucleic acid
GI	Gastrointestinal
MFO	Mixed function oxidase
MRT	Mean residence time
PAH	Polycyclic aromatic hydrocarbons
ppb	Parts per billion
ppm	Parts per million
ppt	Parts per trillion
RNA	Ribonucleic acid
TLV	Threshold limit value
TWA	Time weighted average
UV	Ultraviolet

1. INTRODUCTION

1.1. STRUCTURE AND CAS NUMBER

Chrysene belongs to the class of polycyclic aromatic hydrocarbons (PAH) which are formed as a result of incomplete combustion of organic materials. It is ubiquitous in the environment. Chrysene is also known as 1,2-benzophenanthrene; benzo(a)phenanthrene; and 1,2,5,6-dibenzonaphthalene (IARC, 1973). The structure and substituent numbering system for this compound is depicted below:



The molecular formula for chrysene is $C_{18}H_{12}$ and the molecular weight is 228.28. The Chemical Abstract Service (CAS) Registry number for chrysene is 218-01-9.

1.2. PHYSICAL AND CHEMICAL PROPERTIES

Chrysene is a crystalline solid at room temperature with red-blue fluorescence (IARC, 1973; Weast, 1980) and has the following physical properties:

Melting point:	255-256°C (Weast, 1980)
Boiling point:	448°C (Weast, 1980)
Density at 20°C:	1.274 g/cm³ (Weast, 1980)
Vapor pressure at 25°C:	6.3×10^{-9} mm Hg (Mabey et al., 1981)
Solubility in water at 25°C:	0.002 mg/ℓ (Mackay and Shiu, 1977) 0.0018 mg/kg (May et al., 1978)
Log of soil sorption coefficient standardized with respect to organic carbon content (log K_{oc}):	5.57 (Sabljic and Protic, 1982)

Log octanol/water partition coefficient (log K_{ow}):	5.91-6.01 (Yalkowsky and Valvani, 1979; MacKay et al., 1980)
Henry's Constant (H_C) at 25°C:	1.05×10^{-6} atm. m^3 mol^{-1} (Mabey et al., 1981)

Chrysene is first substituted in the 6 position by electrophilic reactions. It is oxidized to the corresponding 5,6-quinone with boiling chromic acid in glacial acetic acid (IARC, 1973).

1.3. PRODUCTION DATA

Chrysene is not manufactured for industrial purposes in the U.S., but is available as a laboratory reagent from a few commercial sources; however, chrysene is ubiquitous in the environment. A few of the anthropogenic sources of chrysene in the environment are gasoline and diesel vehicular emission (NAS, 1972; Blumer et al., 1977; Yergey et al., 1982); coal combustion and gasification (Nichols et al., 1981); wood burning (Hornig et al., 1981); waste incineration (Beck and Stoebet, 1982); cigarette smoke (Klimisch and Kirchheim, 1976); aircraft turbine exhaust (Spitzer and Dannecker, 1982); various industrial operations, such as iron and aluminum foundry (Bjorseth et al., 1981; Schimberg, 1981), and carbon black manufacture (Serth and Hughes, 1980). Emissions from coke ovens are one of the major industrial sources of chrysene and other PAH (NAS, 1972). Distillate from shale oil and synfuel from solvent refined coal also contain chrysene (Toste et al., 1982). Cooking of food is another anthropogenic source of chrysene in the environment (IARC, 1983). The only likely significant nonanthropogenic sources of PAH (and therefore chrysene) in the environment are forest fires (Kelly, 1983). The amount of PAH released from forest fires was estimated to be 824 metric tons/year, compared with a total man-made estimate of 17,030 metric tons/year (Kelly, 1983). Thus, non-anthropogenic sources of PAH (chrysene) are not very significant.

1.4. USE DATA

There is no known use for this compound other than as a laboratory reagent and in the synthesis of organic chemicals for laboratory use (Hawley, 1981).

2. ENVIRONMENTAL FATE AND TRANSPORT PROCESSES

2.1. WATER

The aquatic fate of chrysene is determined by its ability to undergo photolysis, oxidation and biotransformation/biodegradation and be transported to sediments or the atmosphere. The photolysis of selected PAH including chrysene in water at 25°C was studied by Zepp and Schlotzhauer (1979). The near-surface half-life for direct photolysis of aquatic chrysene by midsummer sunlight at a latitude of 40°N was computed to be 4.4 days. With other conditions remaining the same, the half-life for chrysene was computed to be 13 days at a water depth of 5 m (instead of near-surface). In the presence of 20 mg/ℓ of suspended sediment concentration, the computed half-life increased to 68 days at the same depth (5 m). It can be concluded from the Zepp and Schlotzhauer (1979) study that dissolved chrysene present near the surface of a water-body may undergo photolysis. As will be evident from the discussion below, however, a large portion of the total chrysene in aquatic media is expected to be present in the sorbed state in the sediment and biota and may not undergo significant photolysis. Even the chances of photolysis of dissolved chrysene are expected to decrease as the solution depth increases because of increasing light attenuation at greater water depths.

The oxidation of chrysene in aquatic media by the two most likely reactions, $RO_2\cdot$ radicals and singlet oxygen, does not appear to be a significant fate process. This conclusion is based on the estimated half-lives of ~40 years for both reactions. The half-life estimate for chrysene due to reaction with $RO_2\cdot$ radicals and singlet oxygen present in aquatic media at approximate concentrations of 10^{-9} M and 10^{-12} M (Mill and Mabey, 1980) is based on oxidation rate constants of 10^{3} M^{-1} $hour^{-1}$ and $>10^{6}$ M^{-1} $hour^{-1}$, respectively (Mabey et al., 1981).

Chlorine and ozone used as disinfectants for drinking water can chemically react with PAH present in the water. These reaction rates are not only different for each PAH, but a decrease in pH and an increase in water temperature both increase the rate of degradation. The half-life of benzo(a)anthracene with 2.2 mg/ℓ free chlorine at a pH of 6.8 and a temperature of 20°C was estimated to be 20 minutes, whereas only 20% benzo(k)fluoranthene was degraded in 20 minutes under the same conditions. Similarly, the half-lives of a few PAH such as benzo(a)anthracene and pyrene with ozone in water have been estimated to be in the range of a few minutes (Callahan et al., 1979). While no specific half-life data for chrysene are available, it has been speculated by Callahan et al. (1979) that oxidation by chlorine and ozone may be a significant fate process for chrysene when the concentrations of these oxidants are sufficient (during and subsequent to water treatment as is the case with chlorine and during water treatment as is the case with ozone).

The microbial transformation/degradation rates of a few selected PAH are more comprehensively studied than those of chrysene. It has been reported that biotransformation/biodegradation of PAH with less than four aromatic rings may be an important process in determining the fate of these compounds in aquatic media (Callahan et al., 1979). The biodegradation potential for chrysene in ambient aquatic media, however, remains uncertain. Groenewegen and Stolp (1976) found that chrysene was not measurably degraded by an isolated Pseudomonas species but may be co-oxidized in the presence of other PAH (phenanthrene, pyrene and 1,2-benzanthracene) when passed through a percolation column. The rate of microbial oxidation of chrysene by Pseudomonas putida and Flavobacterium sp. was studied by McKeena (1977). With resting cell suspensions as microbial inoculum, chrysene remained virtually

undegraded by Pseudomonas putida and slightly degraded with Flavobacterium sp. after 4 weeks of incubation. The biodegradability of chrysene was also studied by Tabak et al. (1981) by the static-culture flask-screening procedure with settled domestic wastewater as microbial inoculum. The unacclimatized microorganisms did not biodegrade chrysene substantially. With a 5 and 10 mg/ℓ solution, only 6 and 0%, respectively, of chrysene was found to biodegrade in 7 days. With acclimatized microorganisms, the corresponding amount of biodegradation at the two concentrations was ~60 and ~34%, respectively.

It is difficult to predict the biodegradation half-life of chrysene in natural aquatic systems from the above discussion. The half-life of chrysene in aquatic media, however, can be predicted from the estimated biotransformation rate constant value of 10^{-10} mℓ cell^{-1} hour^{-1} given by Mabey et al. (1981) and the estimated concentration of microorganisms in aquatic media, as 5×10^5 cell mℓ$^{-1}$ (Burns et al., 1981). Under the above assumption, the half-life of chrysene in aquatic media can be estimated to be ~1.5 years. It should be emphasized that this estimated half-life may be valid for aquatic substrate concentrations of <1 ppm (Mabey et al., 1981), and in the case of chrysene, the concentration range in aquatic media could be limited by its solubility of 2 ppt.

The two intramedia processes that may transport chrysene from aquatic media are volatilization to air and sedimentation through sorption on particulate matter and biota. Volatilization of chrysene from aquatic media does not appear to be an important process (Callahan et al., 1979). Judging from the higher log K_{oc} value (5.57), chrysene can be predicted to be readily sorbed by particulate matter including organic substances and fine particles such as clay and silt in the water. In general, PAH compounds

including chrysene deposited on surface water are removed to and incorporated in the organic and inorganic sediments where they are eventually concentrated and have been found by a number of investigators (Gschwend and Hites, 1981; Eadie et al., 1982a). Matsushima (1982) has provided evidence suggesting that the concentration of PAH in sediment increases as the average particle size decreases. Overall, sorption onto particulate matter in water appears to be an important transport process for chrysene.

2.2. AIR

Chrysene, like other PAH, exists in the atmosphere in the particulate-sorbed state. This has been suggested by the mathematical modeling of Natusch and Tomkins (1978), which shows that at ambient temperatures (-10 to 30°C) essentially quantitative adsorption of PAH to particulate matter would be expected. Experimentally, chrysene has been detected exclusively in the air particulate matter by a number of investigators (Santodonato et al., 1981).

The degradation of particle-sorbed chrysene in the atmosphere is likely to depend on its ability to undergo photochemical and other chemical reactions. Photolysis of chrysene adsorbed on four different adsorbents (silica gel G, aluminum oxide G, cellulose powder and acetylated cellulose) by UV and ordinary room light failed to produce any measurable changes (Inscoe, 1964). Falk et al. (1956), however, reported ambiguous results after the photolysis of chrysene in solution in that an 11% degradation was reported for a 24-hour photolysis time and no degradation was reported for a 48-hour photolysis time. Adsorption on air particulate matter, however, seems to have a stablizing effect on the photolysis of PAH in general (Santodonato et al., 1981). Nevertheless, whether particle-associated chrysene is substantially photodegraded in the atmosphere is unknown.

Under certain conditions, a few airborne particulate PAH have been shown to react with SO_2, NO_2 and O_3 to form sulfonic, nitro and oxygenated derivatives, respectively (Santodonato et al., 1981). These reactions have been found to depend both on the nature of PAH and the concentration of the reactant gases. Some of these reactions have been conducted at an unrealistically high reactant gas concentration compared to that expected to be present in the natural atmosphere. Since none of these studies was conducted with chrysene, it is difficult to assess the fate of chrysene in the presence of these reactants at atmospheric concentrations. The study conducted by Falk et al. (1956) showed that 15% of chrysene in unadsorbed form was destroyed in 1 hour when exposed to photochemical smog. The destruction of chrysene, however, was much smaller compared to benzo(a)pyrene under the same conditions (15% versus 50%). This result indicates that in the presence of photochemical smog containing NO_x and O_3, chrysene may undergo some reaction in the atmosphere. The reaction rate in the atmosphere, however, is expected to be slower than in the free form since chrysene is found in the atmosphere in the particle-sorbed form.

The particulate size distribution in urban air follows a bimodal distribution with one mode occurring at lower diameter (~1 μm) and the other at higher diameter (~10 μm). Each mode follows a log normal distribution (Windsor and Hites, 1979). The mass median diameter of particulates that have sorbed chrysene in the winter is slightly lower than in the summer (Pierce and Katz, 1975). The mass diameter of particles in Toronto, Ontario, atmosphere has been determined to be 2.7 and 1.6 μm in summer and winter, respectively (Pierce and Katz, 1975). Van Vaeck et al. (1979), however, calculated a mass median diameter of 0.7-0.9 μm for particles in Belgium-Netherland air. If the particle diameter for atmospheric particles

with sorbed chrysene is assumed to be 1 μm, the dry deposition residence time of such particle under a 4 m/sec wind can be calculated to be 4 days (Windsor and Hites, 1979). The particles will travel 1300 km before settling and will have a half-life of ~3 days. Therefore, chrysene will participate in long distance transport processes in the atmosphere (Daisey and Lioy, 1981; Windsor and Hites, 1979; Lunde and Bjorseth, 1977).

2.3. SOIL

The available literature contained limited information pertaining specifically to the fate of chrysene in soil. The following conclusions regarding the fate of chrysene in soil are derived from the fate of other PAH in soil (Santodonato et al., 1981). Photochemical degradation is unlikely to play any major role in determining the fate of chrysene in soil. Similarly, no other chemical reactions have been shown to play any significant role in the degradation of chrysene in soil. Microbial degradation of chrysene in soil was studied by Groenewegen and Stolp (1976). It was observed that soil microorganisms do not easily degrade chrysene when it is present at ppm level concentration. The microbial degradation of chrysene in soils at even higher concentrations, such as the soils from coke plant and wood preserving plant waste sites, is unknown.

Considering the high soil partition coefficient (K_{oc} = 5.57) and low vapor pressure (6.3×10^{-9} mm Hg), chrysene is not expected to be volatilized significantly from soil. The leaching of chrysene from soil to groundwater is equally improbable because of the low water solubility and high K_{oc}, particularly from soils with high organic carbon content. A large number of monitoring data stored by U.S. EPA in the STORET data base for chrysene concentration in well water, including wells near known and suspected industrial disposal sites, failed to show any detectable level of chrysene (more than the detection limits of <1-20 μg/ℓ of chrysene).

Chrysene in the concentration range of 0.002-0.3 µg/ℓ was detected in a number of impoundment wells around a forest-product producing site in Florence, South Carolina (STORET), thus indicating that chrysene may get into groundwater under some circumstances. Likely reasons for chrysene detection in groundwater are wastewater having a high organic content which may increase the solubility in water and lower the K_{oc}, thus allowing leaching, or direct injection into the aquifer either as a waste disposal practice or inadvertantly with monitoring wells.

3. EXPOSURE

3.1. WATER

Chrysene has been reported to be present in surface water in Germany at concentrations ranging from 11.8-38.2 ng/ℓ (IARC, 1973). The combined chrysene and triphenylene level detected in the effluent from a sewage treatment plant in Norway was 27-184 ng/ℓ (Kveseth et al., 1982). In the U.S., chrysene was detected in trace levels in the influent and effluent of a sewage treatment plant in Philadelphia, Pennsylvania, and in the Delaware River lying just north of Philadelphia (Sheldon and Hites, 1979). Chrysene has been detected in petroleum refinery wastewaters and in the wastewater from coal liquefaction processes (Robbins et al., 1980; Pfeffer, 1979). Other likely important industrial sources of chrysene are wastewaters from coke plants (Santodonato et al., 1981) and wood preserving plants, since creosote used for preserving wood may contain 0.94-1.34 g/kg of chrysene (Lijinsky et al., 1963). Table 3-1 lists some of the sources of chrysene in raw industrial wastewaters (U.S. EPA, 1981). The source of chrysene in iron, steel and aluminum industries is the coke used during the manufacturing process. The level of combined chrysene and triphenylene concentration in Nordic tap water has been determined to be 0.5-7 ng/ℓ (Kveseth et al., 1982). In the U.S., chrysene has been detected but not quantified in drinking water stored in coal tar-coated storage tanks (Alben, 1980a,b). In a laboratory experiment designed to investigate potential water contamination from petroleum asphalt-coated water distribution pipes, Miller et al. (1982) reported a concentration range of <2 ng/ℓ (detection limit) to 5.7 ng/ℓ in the water. Exposure to chrysene through digestion of drinking water cannot be evaluated due to lack of field data in the U.S.

STORET (see Appendix) contains information on 2149 stations of surface water sampled for chrysene (Table 3-2).

TABLE 3-1

Industrial Occurrence of Chrysene[a]

Industry	Raw Wastewater				
	Number of Samples	Number of Detection	Concentration, µg/ℓ		
			Minimum	Maximum	Mean
Coal mining[b]	46	ND	NR	NR	NR
Iron and steel manufacturing[c]	15	12	1	800	<200
Leather tanning and finishing	18	ND	NR	NR	NR
Aluminum forming	5	3	<10	360	<100
Coil coating	78	7	ND	30	10
Electrical/electronic components[d]	4	2	<10	11	<10
Foundries	11	11	4	13,000	2400
Metal finishing[b]	37	3	1	73	25
Photographic equipment/supplies[e]	9	2	1	350	180
Nonferrous metals manufacturing	59	9[f]	ND	10,000	160
Organic chemicals manufacturing/ plastics	NA	8	NA	NA	390

TABLE 3-1 (cont.)

Industry	Raw Wastewater				
	Number of Samples	Number of Detection	Concentration, µg/ℓ		
			Minimum	Maximum	Mean
Paint and ink formulation[c]	NA	NA	NR	10	NR
Petroleum refining[b]	12	NA	ND	<10	ND[g]
Timber products processing	12	8[f]	10	4,700	42[g]

[a]Source: U.S. EPA, 1981

[b]Screening and verification data

[c]Screening data

[d]Data set unspecified

[e]Screening plus additional data

[f]Detections >10 µg/ℓ

[g]Mean calculated using medians

NA = Not available; NR = not reported; ND = not detected

TABLE 3-2

Chrysene Levels in a Few Aquatic Samples

	Total in Water (µg/ℓ)	Dissolved Chrysene (µg/ℓ)	Suspended Particles (µg/ℓ)	Sediment (µg/kg dry weight)	Tissue (mg/kg wet weight)
Number of Samples	1,957	1	2	786	366
Maximum	101,331	10.0	0.060	380,000	70.0
Maximum	ND	10.0	0.002	ND	ND
Mean	130.03	10.0	0.031	3551.6	2.442

ND = Not detected

Chrysene residues have been found at various concentrations in sediments of freshwater and marine environments around the world (Hites et al., 1980). Concentrations of chrysene, triphenylene and benzanthracene were as high as 21.0 mg/kg in sediment from the Charles River, Boston, Massachusetts, while 0.0014 mg/kg was detected in "uncontaminated" intertidal sediment taken near Hitchinbrook Island, Alaska. The lowest levels detected were 0.0002 and 0.0009 mg/kg, taken from sediments of the Amazon River and Rio Negro, respectively (Hites et al., 1980).

Lee et al. (1981) reported chrysene in the sediment of a Georgia salt marsh at 105 mg/kg after a heavy fuel oil spill. The half-life of chrysene, determined by concentrations in mussels, oysters and sediment, was 70 days. Chrysene levels taken from sediment of a river basin, which flows past a coal burning power plant, and from Lake Erie decreased proportionally to their distance from the power plant. Levels in the river sediment approached 0.6 mg/kg, while sediment samples taken 5 and 10 km from the mouth of the river were ~0.2 and 0.1 mg/kg, respectively (Eadie et al., 1982a). Chrysene levels in Lake Michigan sediment were reported to be ~0.8 mg/kg (Eadie et al., 1982b).

Residue levels of chrysene (including triphenylene) reported for sediment samples from the Severn Estuary, England, ranged from 1.1-5.6 mg/kg dry weight (John et al., 1979). Sediments from the Mediterranean coast near Monaco and Cote Bleue contained 0.0092-0.022 mg chrysene/kg dry weight (Mille et al., 1982). Chrysene levels in sediments from Hirakata Bay, Tokyo Bay and rivers flowing into Hirakata Bay ranged from 0.087-1.82 mg/kg dry weight (Matsushima, 1979).

3.2. FOOD

Chrysene has been detected in a wide variety of foods. Although minute amounts of PAH, including chrysene found in foods, are of geochemical and biosynthetic origins, most of the PAH originate in foods from such industrial sources as polluted environments, food additives and packagings, and food processing (Lo and Sandi, 1978). In meat or fish, the amount of chrysene present in the cooked products depends on the method of cooking (broiled, smoked, barbecued, etc.), fat content, heat source and heating temperature. Table 3-3 shows chrysene content in cooked meat and meat products under various conditions of cooking and meat products containing different fat contents.

Chrysene has been detected at a concentration of 2.2 ppb in commercial lobster tail meat before storage and as high as 303 ppb after commercial storage in a tidal pond constructed of creosoted timber (Dunn and Fee, 1979).

In vegetables, chrysene has been detected at a concentration range of 5.7-26.5 ppb in salad, 28.0 ppb in spinach, 0.5 ppb in tomatoes and 58.5-395.0 ppb in kale. In cereals, chrysene has been detected in the range of 0.8-14.5 ppb (IARC, 1973).

Chrysene has also been detected in refined vegetable oils. A level of up to 129 ppb was determined in crude coconut oil and up to 200 ppb in crude coconut fat (IARC, 1973). It has also been detected at a concentration of 0.01-19.1 ppb in roasted coffee or soluble coffee powder and in roasted peanuts at 0.01-0.71 ppb (IARC, 1973; Nistor, 1980). In baker's yeast, a concentration range of 4.2-50 ppb chrysene has been reported (Grimmer, 1974). Chrysene has also been reported in two kinds of whiskey at a concentration range of 0.04-0.06 ppb (IARC, 1973).

TABLE 3-3

Chrysene Concentrations (ppb) in a Few Meat and Meat Products Under Different Conditions

Meat	Method of Cooking	Chrysene Concentration (ppb)	Reference
Steak	charcoal broiled	0.6	Lijinsky and Shubik, 1965
Ribs	barbecued	2.2	Lijinsky and Shubik, 1965
Beef	barbecued	9.6	Freithein, 1976; Panalaks, 1976
Hot sausages	smoked	1.0	Malanoski et al., 1968
Bologna	smoked	0.15-1.20	Freithein, 1976; Panalaks, 1976
Salami	smoked	1.2	Lo and Sandi, 1978
Mortadella	smoked	3.4	Lo and Sandi, 1978
Bacon	heavily smoked	detected	Lo and Sandi, 1978
Hamburger: 21% fat	charcoal broiled at 7 cm from heat source	1.7	Lijinsky and Ross, 1967
7% fat	charcoal broiled in no-drip pan at 7 cm from heat source	trace	Lijinsky and Ross, 1967
T-bone steak	charcoal broiled at 7 cm from heat source	25.4	Lijinsky and Ross, 1967
	flame broiled at 7 cm from heat source	2.0	Lijinsky and Ross, 1967
Ham	lightly smoked	0-3.0	Lo and Sandi, 1978
	heavily smoked	12.0-66.0	Lo and Sandi, 1978

The U.S. EPA (1980) has estimated the weighted average BCF of chrysene in the edible fish and shellfish consumed by Americans as 4620. This estimate is based on the logarithm of the octanol/water partition coefficient for chrysene as 5.61. In benthic organisms, Eadie et al. (1982b) have experimentally determined a BCF of 20,280 for chrysene. Although the levels of chrysene in various foods have been discussed above, it is difficult to estimate the human dietary intake of chrysene unless the chrysene content in a composited diet sample consumed by an average individual in the U.S. is known. The problem is particularly difficult because of different eating habits and methods of cooking among individuals in the U.S.

3.3. INHALATION

The level of chrysene in ambient air, in general, depends on the geographic location, the presence of nearby pollution sources such as vehicular emissions or industrial emissions, and the season. Usually, concentrations are greater in winter than in summer (IARC, 1973). The ambient air concentrations of chrysene at various locations around the world are shown in Table 3-4.

The level of combined chrysene/triphenylene in the air has been reported to be 4.4 $\mu g/m^3$ in stationary samples from an aluminum plant in Norway (Bjorseth et al., 1981).

If the concentration of chrysene in urban U.S. air is assumed to range from 0.6-4.8 ng/m^3 (see Table 3-4), the human daily intake of this compound by inhalation of urban ambient air may be in the range of 11.4-91.2 ng, based on inhalation of 19 m^3 of air/day.

TABLE 3-4

Atmospheric Chrysene Levels at Various Locations Around the World

Location	Chrysene Concentration (ng/m^3)	Reference
Detroit, MI	1.3-11.6	Hoffmann and Wynder, 1968
Rome, Italy	3.4-15.0	Liberti et al., 1975
College Park, MD	4.8	Fox and Staley, 1976
Budapest, Hungary	7.2	Kertesz-Saringer and Morlin, 1975
Los Angeles, CA	0.60	Gordon, 1976
Sidney, Australia	0.2-6.7	Hoffman and Wynder, 1977
Baltimore Harbor Tunnel, MD	106	Fox and Staley, 1976
New York City, NY	ND-2.4*	Daisey et al., 1979
Patten, the Netherlands	0.07-0.43*	Broddin et al., 1980
Botrange (rural), Belgium	0.23 (summer)* 0.48 (winter)*	Broddin et al., 1980
Antwerp (urban), Belgium	8.5 (summer)* 94.7 (winter)*	Broddin et al., 1980

*These values represent concentrations of chrysene with another isomer that could not be separated.

ND = Not detected

3.4. DERMAL

Two likely sources of dermal exposure to chrysene are coal tar from manufacturing and user industry, and creosote from the wood preserving industry, since creosote may contain 0.94-1.27 g/kg of chrysene, and coal tar may contain 2.13-2.86 g/kg of chrysene (Lijinsky et al., 1963). Pertinent data to evaluate the dermal exposure from these sources could not be located in the available literature.

4. PHARMACOKINETICS

4.1. ABSORPTION

As a class, PAH are well absorbed through the GI and respiratory tracts of rodents (U.S. EPA, 1980). That chrysene was absorbed from the GI tract of female CD-COBS rats can be inferred from the distribution of chrysene in blood, liver, brain, mammary and adipose tissue (see Section 4.2.) following oral administration of the chemical at 22.8 or 11.8 mg/rat in 2 mℓ olive oil (Modica et al., 1983). The rats eliminated 37.6 and 25.4% of the high and low doses, respectively, in the 72-hour feces, indicating that at least 62.4 and 74.6% of the respective dose was absorbed.

4.2. DISTRIBUTION

Modica et al. (1983) treated female CD-COBS rats with chrysene in olive oil and Pluronic F68 (an emulsifier) by gavage at doses of 11.4 or 22.8 mg/rat. The rats were sacrificed at intervals for 24 hours and samples of arterial blood, mammary tissue, parametrial adipose tissue, liver and brain were collected and analyzed for chrysene. The AUC and MRT for the tissues were calculated from kinetic parameters. The values for AUC (hours • µg/mℓ blood or g tissue) and MRT (hours) for the two dose levels are presented in Table 4-1. As seen for the AUC and MRT values at 22.8 mg/rat, adipose tissue had, by far, the greatest affinity for and retention of chrysene, followed by mammary tissue, brain, liver and blood. A similar pattern was obtained with half the dose. The investigators suggested that at the higher dose, saturation of GI absorption, precipitation of chrysene or deposition of chrysene in tissues not examined may have contributed to the lack of a dose relationship in the AUC.

TABLE 4-1

AUC and MRT of Chrysene in Tissues of Female Rats*

Dose	Blood		Liver		Brain		Mammary Tissue		Adipose Tissue	
	AUC	MRT	AUC	MRT	AUC	MRT	AUC	MRT	AUC	MRT
22.8 mg/rat	0.42	2.13	2.46	3.43	5.73	4.19	12.16	7.11	66.82	11.44
11.4 mg/rat	0.49	1.60	2.30	2.22	4.06	3.42	4.04	4.71	91.88	12.01

*Source: Modica et al., 1983

4.3. METABOLISM

Berenblum and Schoental (1949) identified 3-hydroxychrysene as a metabolite of chrysene in the feces of rats injected intraperitoneally with 25 mg chrysene/rat. Harper (1959) concluded that the conjugates found in the feces of mice following intravenous injection of 0.5 mg chrysene were 3-chrysenyl sulfate and 3-chrysenyl glucuronide.

Recently, the metabolism of chrysene by rat liver microsomal MFO systems has been studied in vitro. Metabolites have been identified as 4 or 5 isomeric hydroxychrysenes; 1,2-dihydro-1,2-dihydroxychrysene; 3,4-dihydro-3,4-dihydroxychrysene; and slight amounts of 5,6-di-hydro-5,6-dihydroxychrysene (the K-region dihydrodiol). The dihydrodiols are formed through the intermediate formation of reactive epoxides (MacNicoll et al., 1979; Sims, 1970; Nordqvist et al., 1981; Jacob et al., 1982). Jacob et al. (1982) reported that rat liver microsomes oxidize chrysene at the 1,2- and 3,4-position (the 3,4-position predominates) to yield the 1,2- and 3,4-dihydrodiols and 1- and 3-hydroxychrysene. No 5,6-dihydrodiol was found. Incubation of chrysene with microsomes from rats pretreated with various MFO inducers, including phenobarbital, polychlorinated biphenyl, benzoflavone or other PAH, resulted in secondary oxidation products detected as triols, which the investigators believed to be formed from conversion of dihydrodiol epoxides during extraction and handling procedures. The 1,2-dihydroxy-3,4-epoxy-1,2,3,4-tetrahydrochrysene (detected as 1,2,3-triol) is believed to be the ultimate carcinogen, while the 1,2-dihydrodiol is believed to be the proximate carcinogen.

Hamster embryo cells were incubated with ^{3}H-chrysene and the RNA was extracted and hydrolyzed (Hodgson et al., 1983). Chromatographic analysis indicated that a bay region 1,2-dihydroxy-3,4-epoxy-1,2,3,4-tetrahydrochrysene-N^{2}-guanine adduct in RNA had been formed.

In addition to metabolism of chrysene in the liver, MacNicoll et al. (1980) reported that incubation of ^{3}H-chrysene with mouse skin tissue cultures resulted in the formation of predominantly the 3,4-dihydrodiol, as well as the 1,2- and 5,6-dihydrodiols.

4.4. EXCRETION

Harper (1959) found that in mice injected intravenously with 0.5 mg chrysene, excretion occurred predominantly via the bile into the feces. Female CD-COBS rats eliminated 37.6 and 25.4% of orally administered chrysene at doses of 22.8 and 11.4 mg/rat, respectively, in the 72-hour feces (Modica et al., 1983). These findings are in agreement with the observed rapid elimination in the feces of other closely related PAH (U.S. EPA, 1980).

5. EFFECTS

5.1. CARCINOGENICITY

Studies on the carcinogenic effect of oral or inhalation exposure to chrysene could not be located in the available literature. Studies in which chrysene was administered to rodents by skin painting, intraperitoneal or subcutaneous injection have been performed and provide some information on the carcinogenicity of this compound. Studies of the carcinogenicity of chrysene in animals have been reviewed by IARC (1973, 1983). IARC (1983) reports that the evidence for the carcinogenicity of chrysene in animals is limited.

Skin painting experiments in which chrysene has been assessed as a tumor initiator (incomplete carcinogen requiring the aid of a promoter) and as a complete carcinogen are summarized in Tables 5-1 and 5-2, respectively. Positive results for tumor initiation on mouse skin were obtained by Chang et al. (1983), El-Bayoumy et al. (1982), Wood et al. (1979), Hecht et al. (1974), Scribner (1973) and Van Duuren et al. (1966). As a complete carcinogen on mouse skin, both positive (Hecht et al., 1974; Wynder and Hoffmann, 1959) and negative (Horton and Christian, 1974; Hoffmann et al., 1974; Van Duuren et al., 1966) results were obtained. Details of the experiments are provided in Tables 5-1 and 5-2. For completeness, an early study (Bachmann et al., 1937) is included.

Table 5-3 summarizes experiments in which chrysene was administered to various strains of mice by either intraperitoneal or subcutaneous injection.

TABLE 5-1

Summary of Studies Testing for Initiating Activity of Chrysene in Mice - Dermal Application

Strain/ Sex	No. of Animals[a]	Dose and Schedule of Application	Promoter	Time Interval for Last Initiator to First Promoter	Dose and Schedule of Promoter	Tumor Type	Tumor[b] Incidence	Reference
CD-1/F	30	1.2 µmol/200 µl 10% DMSO in acetone	TPA	7 days	16 nmole in 200 ml acetone, twice weekly for 25 weeks	papilloma	13/30	Chang et al., 1983
	30	0.4 µmol/200 µl 10% DMSO in acetone				papilloma	13/30	
	30	0 µmol/200 µl 10% DMSO in acetone (single applications)				papilloma	3/30	
Crl/CD-1 (ICR) BR/F	20	10x0.1 mg/0.1 ml acetone	TPA	10 days	2.5 µg in 0.1 ml acetone 3 times/week for 25 weeks	squamous cell carcinoma	20/20 p<0.01	El-Bayoumy et al., 1982
	20	control-10x0.1 ml acetone (every other day)				squamous cell carcinoma	1/20	
CD-1/F	30	2 µmol/200 µl 10% DMSO in acetone	TPA	7 days	16 nmol in 200 ml acetone twice weekly for 25 weeks	papilloma	20/30	Wood et al., 1979
	30	0/200 µl 10% DMSO in acetone (single applications)				papilloma	3/30	
HA/ICR/F	20	10x0.1 mg in 0.1 acetone	TPA	10 days	2.5 µg in 0.1 ml 3 times/week for 30 weeks	NR	11/18	Hecht et al., 1974;
	20	control - 10x0.1 ml				NR	0/20	Hoffmann et al., 1974
	20	acetone (every other day)						
CD-1/F	30	4.4 µmol in acetone	TPA	7 days	5 µmol 2 times/week for 35 weeks	papilloma	22/30	Scribner, 1973
	30	0 µmol in acetone (single application)				papilloma	1/30	
HA/ICR/F	20	1 mg in 0.4 ml acetone	croton resin	13-21 days	25 µg in 0.1 ml acetone 3 times/ week for 60 weeks	papilloma	16/20	Van Duuren et al., 1966
	20	0 mg in 0.4 ml (single application)				carcinoma	2/20	
						papilloma	5/20	
						carcinoma	1/20	

[a]Number of animals - initial number of experimental animals in most cases

[b]Tumor incidence is expressed in terms of number of tumor-bearing animals/number of effective animals surviving, whenever possible.

NR - Not reported

TPA - Tetradecanoyl phorbal acetate

DMSO - Dimethyl sulfoxide

TABLE 5-2

Summary of Studies Testing for Complete Carcinogenicity of Chrysene in Mice - Dermal Application

Strain/Sex	No. of Animals[a]	Dose and Schedule of Application	Tumor Type	Tumor Incidence[b]	Reference
C3H/M	20	50 mg in 60 µℓ of decalin[c]	papilloma carcinoma	1/12 0/12	Horton and Christian, 1974
HA/ICR/MIL/F	20	0.1 mg in 0.1 mℓ acetone 3x weekly for 30 weeks	NR	0/20	Hoffmann et al., 1974
	20	0.1 mℓ acetone 3x weekly for 30 weeks	NR	0/20	
HA/ICR/MIL/F	20	0.1 mg in 0.1 mℓ acetone 3x weekly for 17 months	papilloma	4/18	Hecht et al., 1974
	20	0.1 mℓ acetone 3x weekly for 17 months	papilloma	0/20	
ICR/HA/MIL/F	20	1 mg in 0.4 mℓ acetone single application	papilloma carcinoma	0/20 0/20	Van Duuren et al., 1966
	20	0 mg in 0.4 mℓ acetone	papilloma carcinoma	0/20 0/20	

TABLE 5-2 (cont.)

Strain/Sex	No. of Animals[a]	Dose and Schedule of Application	Tumor Type	Tumor Incidence[b]	Reference
Swiss/MIL/F	20	1% in acetone 3x weekly for 13 months[c]	papilloma carcinoma	9/20 8/20	Wynder and Hoffman, 1959
NR	20	0.3% in benzene 2x weekly for 122 weeks[c]	papilloma	1/6	Bachmann et al., 1937

[a]Number of animals = initial number of experimental animals in most cases.

[b]Tumor incidence is expressed in terms of number of tumor-bearing animals/number of effective animals surviving, whenever possible.

[c]No concurrent vehicle controls were used.

NR = Not reported

TABLE 5-3

Summary of Chrysene Carcinogenicity Studies Using Intraperitoneal or Subcutaneous Routes of Administration

Species/Strain	Route	Sex	No. of Animals[a]	Dose and Schedule of Injection	Vehicle	Duration of Study	Tumor Site	Tumor Incidence[b]	Reference
Mouse/ BLU:Ha(ICR)	i.p.	M	40	1.4 µmole divided into 3 doses: 0.2, 0.4 and 0.8 µmole injected on days 1, 8 and 15 of life, respectively	DMSO	37-41 weeks	lung liver	4/27 6/27	Chang et al., 1983
		F	40		DMSO	37-41 weeks	lung liver	1/11 0/11	
		M	60	0	DMSO	37-41 weeks	lung liver	4/52 0/52	
		F	60	0	DMSO	37-41 weeks	lung liver	6/41 0/41	
Mouse/ BLU:Ha(ICR)	i.p.	M	50	1.4 µmoles divided into 3 doses: 0.2, 0.4 and 0.8 µmole injected on days 1, 8 and 15 of life, respectively	DMSO	38-42 weeks	lung liver	5/24 6/24	Buening et al., 1979
		F	50		DMSO	38-42 weeks	lung lung	1/11 0/11	
		M	50	0	DMSO	38-42 weeks	lung liver	2/21 0/21	
		F	50	0	DMSO	38-42 weeks	lung liver	7/38 0/38	
Mouse/Swiss	s.c.	M	52	3 x 0.1 mg in 0.02 ml PEG on days 1, 2 and 3 of life	PEG	70-75 weeks	lung liver	1/27 3/27	Grover et al., 1975
		F	52		PEG	70-75 weeks	lung liver	1/21 0/21	
		M	48	0	PEG	70-75 weeks	lung liver	3/30 9/30	
		F	48	0	PEG	70-75 weeks	lung liver	1/15 0/15	
Mouse/C57 Bl	s.c.	M	20	10 x 1 mg, weekly	arachis oil	262 days	NR	2/20	Boyland and Sims, 1967
		M	20	0	arachis oil	262 days	NR	0/20	
Mouse/C57 Bl	s.c.	M/F	40	5 mg in 0.5 ml tricaprylin single injection[c]	tricaprylin	22-28 months	injection-site sarcoma	5/22	Steiner, 1955
Mouse/C57 Bl	s.c.	M/F	50	5 mg in 0.5 ml tricaprylin single injection	tricaprylin	22 months	injection-site sarcoma	4/24	Steiner and Falk, 1951
		M/F	304	0 mg in 0.5 ml tricaprylin single injection	tricaprylin	22 months	injection-site sarcoma	3/233	
		M/F	130	uninjected	NA	22 months	injection-site sarcoma	0/114	

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TABLE 5-3 (cont.)

Species/Strain	Route	Sex	No. of Animals[a]	Dose and Schedule of Injection	Vehicle	Duration of Study	Tumor Site	Tumor Incidence[b]	Reference
Mouse/strain A	s.c.	M/F	30	2 x 10 mg, 4 months apart[c]	lard	15 months	injection-site sarcoma	0/30	Shear and Leiter, 19[illegible]
Rat/strain NR	s.c.	NR	10	0.05% in 2 mL aqueous colloidal solution[c]	water	103 weeks	NR	1/10	Boyland and Burrows, 1935
Rat/strain NR	s.c.	NR	10	2 mg/mL: 1 mL weekly, then 3 mL at longer intervals	lard	626 weeks	injection-site sarcoma	4/10	Barry and Cook, 1934
		NR	10	0 mg/mL: 1 mL weekly, then 3 mL at longer intervals	lard	626 weeks	injection-site sarcoma	2/10	
Mouse/ strain NR	s.c.	NR	10	2 mg/mL: 0.5 mL weekly then 1 mL at longer intervals	lard	350 days	injection-site sarcoma	0/10	Barry and Cook, 1934
		NR	20	0 mg/mL: 0.5 mL weekly then 1 mL at longer intervals	lard	350 days	injection-site sarcoma	0/20	
Mouse/ strain NR	s.c.	M/F	50	1 injection 0.5 mL (0.4% in lard)[c]	lard	45 weeks	injection-site sarcoma	0/50	Bottomley and Twort, 1934
Mouse/ strain NR	i.p.	M/F	50	1 injection 0.5 mL (0.4% in lard)[c]	lard	50 weeks	injection-site sarcoma	0/50	Bottomley and Twort, 1934

[a]Number of animals = initial number of experimental animals

[b]Tumor incidence is expressed in terms of number of tumor-bearing animals/number of effective animals surviving, whenever possible.

[c]No concurrent vehicle controls were used.

NA = Not applicable; NR = not reported; PEG = polyethylene glycol; DMSO = dimethylsulfoxide; s.c. = subcutaneous; i.p. = intraperitoneal

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An increased incidence of hepatic tumors (significance not determined), but not pulmonary tumors, were found in male mice following intraperitoneal injections of chrysene when compared with controls (Chang et al., 1983; Buening et al., 1979). The incidence of pulmonary and hepatic tumors did not appear to differ greatly from control values following subcutaneous administration of the chemical (Grover et al., 1975). Injection site tumors were induced following subcutaneous injections in mice (Boyland and Sims, 1967; Steiner, 1955; Steiner and Falk, 1951) and rats (Barry and Cook, 1934). Negative results were obtained in some older studies (Shear and Leiter, 1941; Bottomley and Twort, 1934; Barry and Cook, 1934), which are included to show completeness. Experimental details of the above studies are given in Table 5-3.

5.2. MUTAGENICITY

The mutagenic potential of chrysene has been well studied in microbial assays and in mammalian cell systems. Table 5-4 summarizes many of these studies. Chrysene gave positive results in the Ames Salmonella typhimurium assay in the presence of activating systems (Guthrie et al., 1982; LaVoie et al., 1979; Florin et al., 1980; McCann et al., 1975); however, negative results were also reported (Rosenkranz and Poirier, 1979; Simmon, 1979a; Simmon et al., 1979; Basler et al., 1977; Wood et al., 1977). Chrysene was positive for resistance to 8-azaquanine in S. typhimurium strain TM677 (Kaden et al., 1979) but negative for DNA modifying capacity in Escherichia coli (Rosenkranz and Poirier, 1979) and for recombination in Saccharomyces cerevisiae (Simmon, 1979b; Simmon et al., 1979).

In mammalian systems, chrysene administration in vivo produced sister chromatid exchange in Chinese hamster cells (Roszinsky-Kocher et al., 1979), and chromosome aberrations in mouse oocytes and hamster spermatogonia, but not in hamster bone marrow cells (Basler et al., 1977). In vitro incubation

TABLE 5-4

Summary of Mutagenicity Testing of Chrysene

Assay	Indicator Organism	Application	Concentration or Dose	Activation System	Response[a]	Comment	Reference
Reverse mutation	Salmonella typhimurium TA100	plate incorporation	0, 10, 30 and 100 µmol/plate	+ RSV ± S9	- ±	RSV-microsomes from ram seminal vesicals + at ≥10 µM/plate	Guthrie et al., 1982
Reverse mutation	S. typhimurium TA98 TA100	plate incorporation	5-100 µg/plate	+ S9 + S9	+	+ at least 1.8 times solvent (DMSO) control. Maximum dose-response at 20 µg/plate. It was not clear for which tester strain the test was +.	LaVoie et al., 1979
Reverse mutation	S. typhimurium TA98 TA100	plate incorporation	0-1.5 µmol/plate	± S9 ± S9	- ±	NC	Florin et al., 1980
Reverse mutation	S. typhimurium TA1535 TA1538	plate incorporation	0-250 µg/plate	± S9 ± S9	- -	NC	Rosenkranz and Poirier, 1979
Reverse mutation	S. typhimurium TA1535 TA1536 TA1537 TA1538	plate incorporation	0-1000 µg/plate (43.8 µmol)	± S9 ± S9 ± S9 ± S9	- - - -	NC	Simmon, 1977a
Reverse mutation host mediated	S. typhimurium TA1530 TA1538 TA1538	intramuscular injection into host mice oral administration to host mice	125 mg/kg 300 mg/kg	NA NA	- - -	NC	Simmon et al., 1979
Reverse mutation	S. typhimurium TA1535 TA98	plate incorporation	1, 10 or 100 µg/plate	± S9 ± S9	- -	NC	Basler et al., 1977

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TABLE 5-4 (cont.)

Assay	Indicator Organism	Application	Concentration or Dose	Activation System	Response*	Comment	Reference
Reverse mutation	S. typhimurium TA98	NR	0-125 nmole/ plate	± S9	-	NC	Wood et al., 1977
	TA100			± S9	-		
	TA98	NR	37.5 nmole/ plate	± purified cytochrome P-450	-		
	TA100				-		
Reverse mutation	S. typhimurium TA98	NR	10 µg/plate	+ S9	+	NC	McCann et al., 1975
	TA100			+ S9	+		
Forward mutation (resistance to 8-azaquanine)	S. typhimurium TM677	2 hour incubation	45 µM	+ S9	+	The concentration was the lowest concentration for significantly induced mutation.	Kaden, 1979
DNA modifying capacity	Escherichia coli pol A+ pol A-	liquid incubation	250 µg/mL	+ S9	-	Survival index = 1.07; pol A- strain was not inhibited preferentially.	Rosenkranz and Poirier, 1979
Mitotic recombination	Saccharomyces cerevisiae	plate incorporation	5% wt/vol highest dose	± S9	-	No recombinants	Simmon, 1979b
Mitotic recombination host-mediated	S. cerevisiae D3	oral administration to host mice	330 mg/kg	NA	-	NC	Simmon et al., 1979
Induction of spindle shaped cells	ICR mouse embryonic cells	incubation with cell culture	0.14-225 µM	NA	-	NC	Kamei, 1980
Chromosome aberrations	NMRI strain mice metaphase II oocytes	oral administration	450 mg/kg	NA	+	Weakly positive: 0.82% chromosome aberrations in controls vs. 5.56% in treated mice (P<0.04).	Basler et al., 1977
Chromosome aberrations	Chinese hamster spermatogonial chromosomes	oral by gavage	2 x 450 mg/kg in 24 hours	NA	+/-	low but not significant increase in aberrations	Basler et al., 1977

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TABLE 5-4 (cont.)

Assay	Indicator Organism	Application	Concentration or Dose	Activation System	Response*	Comment	Reference
Chromosome aberrations	Chinese hamster bone marrow	gavage	2 x 450 mg/kg in 24 hours	NA	-	NC	Basler et al., 1977
		gavage or intraperitoneally	5 x 450 mg/kg in 24 hours	NA	-		
Sister chromatid exchange	Chinese hamster	intraperitoneally	2 x 450 mg/kg in 24 hours	NA	+	p<0.02; 5.1 ± 1.0 SCE/metaphase vs. 3.9 ± 0.9 for controls	Roszinsky-Kocher et al., 1979
Resistance to oubain	Chinese hamster V79 embryo cells	incubation with cell culture	1-10 µg/mℓ for 2 days	±2° cultured whole golden hamster embryo cells	=	NC	Huberman and Sachs, 1976
Resistance to B-azoquanine	Chinese hamster V79 embryo	incubation with cell culture	1-10 µg/mℓ for 2 days	±2° cultured whole golden hamster embryo cells	=	NC	Huberman and Sachs, 1976
Cell transformation	Syrian hamster fetal lung cells	incubation for 24 hours	0.05, 0.1, 0.25, 0.5, 0.75, 1.0 µg/mℓ	NR	-	NC	Richter-Reichhelm et al., 1979
Colony transformation	Syrian hamster embryo cells	culture incubated 4 hours	5-15 µg/mℓ	feeder layer of rat fibroblasts	-	NC	Huberman et al, 1972
Hepatocyte primary culture (HPC) DNA Repair	rat, HPC	18-20 hour incubation	1×10^{-4} M 5×10^{-4} M 1×10^{-3} M	NA	-	No increase in ^{3}H TdR uptake	Tong et al., 1981

*Responses: +, positive; -, negative; =, negative with and without S9 activation system; ±, positive with and negative without S9 activation system; ∓, negative with and positive without S9 activation system

NA = Not applicable; NR = Not reported; NC = No comment

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of chrysene with mammalian cell systems produced negative results with respect to resistance to 8-azaquanine and to ouabain in Chinese hamster V79 embryo cells (Huberman and Sachs, 1976), cell transformation capacity in Syrian hamster fetal lung cells (Richter-Reichhelm et al., 1979) and Syrian hamster embryo cells (Huberman et al., 1972), induction of spindle-shaped cells in mouse embryo cultures (Kamei, 1980) and DNA repair in rat hepatocyte primary cultures (Tong et al., 1981). Details of these mutagenicity assays are given in Table 5-4.

5.3. TERATOGENICITY

Pertinent data regarding the teratogenicity of chrysene could not be located in the available literature.

5.4. OTHER REPRODUCTIVE EFFECTS

The only information regarding other reproductive effects of exposure to chrysene is a report that oral administration of 60 mg chrysene/kg to pregnant rats on the 19th day of gestation resulted in the induction of benzo-(a)pyrene hydroxylase and aminoazo dye N-demethylase in fetal livers (Welch et al., 1972).

5.5. CHRONIC TOXICITY

Pertinent data regarding the toxic effects of chronic or subchronic exposure to chrysene could not be located in the available literature.

5.6. OTHER RELEVANT INFORMATION

Schmid et al. (1967) reported that a single intraperitoneal injection of 7.5 mg chrysene/mℓ sesame oil to AKR/J and C57BL/6J mice produced no evidence of toxic effects during a 20-day observation period or upon necropsy at the end of the experiment.

Intragastric administration of 100 mg chrysene/kg to male Wistar rats for 4 days resulted in a 3-fold increase in the activity of liver cytosolic aldehyde dehydrogenase (Torronen et al., 1981).

Chrysene was found to induce aryl hydrocarbon hydroxylase (AHH, a mixed function monoxygenase) when 25 μM chrysene was incubated for 24 hours with cultured human lymphocytes (Snodgrass et al., 1979); however, Gurtoo et al. (1979) failed to find an effect by chrysene on the activity of AHH in cultured human lymphocytes. A single topical application of 1 mg chrysene/ 10 g (body weight) to neonatal rats resulted in induction of AHH as well as 7-ethoxycoumarin O-deethylase in liver and skin (Mukhtar et al., 1982).

Huggins et al. (1964) found that repeated feeding of chrysene (15 mg x 16 days) to female Sprague-Dawley rats had a protective effect on the carcinogenicity of concurrently administered 7,12-dimethylbenz(a)anthracene, reducing the incidence and increasing the time of appearance of mammary tumors.

6. AQUATIC TOXICITY

6.1. ACUTE TOXICITY

The effects of exposure to chrysene for a period of 24 hours at 5.0 mg/ℓ in aerated water at 55°F were examined in rainbow trout, Salmo gairdneri, bluegill sunfish, Lepomis macrochirus, and larval lampreys, Petromyzon marinus (Applegate et al., 1957). No effect of the chemical was noted in any fish species at 5 mg/kg water. Testing was conducted for 24 hours and usually two fish of each species were used in the tests.

6.2. CHRONIC EFFECTS

Pertinent data regarding the effects of chronic chrysene exposure to aquatic organisms could not be located in the available literature.

6.3. PLANT EFFECTS

Chrysene administered in algal media at 62-96% saturation levels (measured concentration not reported) reduced the growth of the blue-green alga, Anabaena flosaquae, ~35% during 14 days of exposure (Bastian and Toetz, 1982). Chrysene exposure at an undetermined level stimulated growth of sporelings of the marine alga, Antithamnion plumula (Boney, 1974).

6.4. RESIDUES

Chrysene residues were determined to be 0.061 and 0.006 mg/kg in bullhead catfish, Ictalurus nebulosus, taken from the Black River (industrial region of Ohio) and Buckeye Lake, respectively (Vassilaros et al., 1982). A striped bass, Morone saxatillis, from the Potomac River contained 0.003 mg chrysene/kg. Eadie et al. (1982b) reported chrysene residues at 0.6 in the amphipod, Pontoporeia hoyi, from Lake Michigan. Mussels, Mytilus edulis, collected off the coast of Norway had chrysene levels ranging from 0.078-0.726 mg/kg, while tissue levels in the periwinkle, Littorina littorea, and limpet, Patella vulgata, ranged from 0.015-0.169 and 0.041-0.938 mg/kg,

respectively (Knutzen and Sortland, 1982). Mussels, M. edulis, collected near the effluent of a sewage treatment plant in Oslo, Norway, had 0.045-0.070 mg chrysene/kg (Kveseth et al., 1982).

6.5. OTHER RELEVANT INFORMATION

Chrysene injected intraperitoneally at ~30 mg/kg (single injection) in rainbow trout, S. gairdneri, increased hepatic cytochrome P-450 levels and aniline hydroxylase activity. Aryl hydrocarbon hydroxylase activity was not significantly altered after chrysene treatment (Gerhart and Carlson, 1978).

7. EXISTING GUIDELINES AND STANDARDS

7.1. HUMAN

No established exposure criteria for chrysene were located in the available literature. PAH as a class, however, are regulated by several authorities. The World Health Organization (WHO, 1970) has recommended that PAH concentration in drinking water not exceed 0.2 µg/mℓ. The U.S. EPA (1980) has recommended an ambient water quality criterion for PAH of 28 ng/ℓ, which is estimated to correspond to an increase in human cancer risk of 10^{-5} over the lifetime.

Occupational exposure criterion for coke oven emissions is 0.15 mg/m³ for the benzene-soluble fraction of total particulate matter (NIOSH, 1978). The TLV-TWA for coal tar pitch volatiles and particulate PAH adopted by the ACGIH (1980, 1982) is 0.20 mg/m³. The ACGIH (1982) lists chrysene as an industrial substance suspect of carcinogenic potential for man, but does not recommend a TLV specifically for chrysene.

7.2. AQUATIC

Guidelines and standards for the protection of aquatic organisms from the toxic effects of chrysene were not located in the available literature.

8. SUMMARY AND CONCLUSIONS

As described in Section 5.1., chrysene has been studied for carcinogenicity following subcutaneous or intraperitoneal injection in rodents. In these assay systems exposure to chrysene has resulted in increases in the number of tumor-bearing animals. Either a single or a limited number of applications of chrysene to the skin of mice followed by repeated application of a tumor-promoting agent resulted in substantial increases in tumor-bearing animals. In tests of chrysene for complete carcinogenic action on mouse skin, the Wnyder and Hoffman (1959) study suggests a weakly positive response. This evidence indicates that cnrysene is a tumor-initiating agent in the mouse skin two-stage tumorigenesis model and suggests that chrysene may be a complete carcinogen. Since no appropriate studies were found on the carcinogenicity of chrysene following oral or inhalation exposure, a human carcinogenic potency factor (q_1^*) cannot be calculated.

The majority of mutagenicity and genotoxicity assays performed on chrysene have yielded negative results (see Table 5-4). In a few instances, chrysene produced mutations in S. typhimurium TA100, TA98 or TM677 in the presence of a metabolic activating system, and chromosomal aberrations or sister-chromatid exchange in mammalian cells. No information regarding the potential teratogenicity of this compound was available.

No information was encountered on the effects of chronic or subchronic exposure to chrysene by any route; therefore, the calculation of a value for an ADI is not possible.

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APPENDIX

LITERATURE SEARCHED

This profile is based on data identified by computerized literature searches of:

CA SEARCH (Files 308, 309, 310, 311, 320)
TOXLINE
MEDLINE
RTECS
SCI SEARCH
OHM TADS
STORET
SRC Environmental Fate Data Bases
SANSS
AQUIRE

Most of these searches were conducted in June, 1983. In addition, hand searches were made of Chemical Abstracts (Collective Indices 6 and 7th), and the following secondary sources were reviewed:

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